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BY CM/ECF
The Honorable Richard G. Andrews
United States District Court for the District of Delaware
844 N. King Street
Wilmington, DE 19801

Re: *United Therapeutics Corp. v. Liquidia Technologies, Inc.*
C.A. No. 23-975-RGA-SRF

Dear Judge Andrews:

Further to the Court's September 24, 2025 oral order, Defendant Liquidia Technologies, Inc. ("Liquidia"), submits the following letter brief explaining why the Federal Circuit's decision in *Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.,* No. 2023-2434, 2025 WL 2698408 (Fed. Cir. Sept. 23, 2025) ("*Bayer*") supports Liquidia's position that the clinical trial results recited in claims 5, 6, 9 and 17 of U.S. Patent No. 11,826,327 ("'327 patent") are not entitled to any patentable weight when determining anticipation and obviousness of the '327 patent.

I. INTRODUCTION

Claim 1 of the '327 patent is directed to a method of improving exercise capacity in PH-ILD patients by administering at least 15 micrograms of treprostinil up to a maximum tolerated dose, via inhalation, in a single administration event that comprises 6 micrograms per breath. JTX1, Claim 1. As proven at trial and discussed in Liquidia's post-trial briefing, claim 1 literally encompasses the known-since-2009 method of administering Tyvaso, according to the Tyvaso label, to PH-ILD patients to obtain the same improvement in exercise capacity that was observed by doctors and disclosed in the prior art. Dependent claims 5, 6, 9 and 17 are merely clinical observations UTC made after completing the phase III INCREASE study, which was conceived

by Dr. Waxman, who encouraged UTC in 2015 to proceed with the trial based on his use of Tyvaso in PH-ILD patients at Brigham and Women's Hospital, published in Agarwal (DTX161) and Faria-Urbina (DTX348; DTX505).

UTC admits that claims 5, 6, 9 and 17 cover nothing more than the clinical benefits that were observed upon completion of the INCREASE trial. D.I. 426, 4. UTC advocates in its post-trial briefing, citing its expert Dr. Nathan, that nothing needs to be done to infringe these claims other than perform the method of claim 1: no measurements, no observations, no statistical analysis, and in fact, the outcomes need not even be experienced by the PH-ILD patient because they are automatically infringed. Claims 5, 6, 9 and 17 are simply the intended results of the method of claim 1. Tr. 142:3-6; D.I. 425, 3. UTC's and Dr. Nathan's positions at trial further reinforce the fact that the clinical outcomes encompassed by these dependent claims are not entitled to patentable weight. D.I. 424, § III; D.I. 425, § III; D.I. 429, § VII; D.I. 435, 1. Accordingly, when assessing anticipation and obviousness of the '327 patent, if claim 1 is found invalid, then so too are claims 5, 6, 9 and 17.

The Federal Circuit's recent decision in *Bayer*, which addressed whether the claimed phrase "clinically proven effective"—a result observed in a clinical trial—added patentable weight, speaks directly to this point as Bayer's claim is substantively indistinguishable from the results observed in claims 5, 6, 9 and 17, and supports Liquidia's position. The *Bayer* case addresses the same type of clinical trial patent claims as the '327 patent and rejects the same validity arguments UTC makes.

II. BAYER'S '310 PATENT CLAIMS ARE DIRECTED TO THE SAME TYPE OF CLINCIAL TRIAL RESULTS DISCLOSED AND CLAIMED IN THE '327 PATENT

As stated by the Federal Circuit, Bayer's '310 patent "describes the results of a phase III clinical trial called 'COMPASS' that evaluated the efficacy and safety of administering rivaroxaban with and without aspirin for the prevention of major adverse cardiac events." *Bayer*, 2025 WL 2698408, at *1.

Similarly, the '327 patent discloses and claims the results from UTC's phase III INCREASE study as acknowledged by UTC:

- "The '327 patent describes INCREASE data in the specification and is listed in the Orange Book for Tyvaso." D.I. 427, ¶ 6.
- "Claims 5, 6, 9 and 17 are supported in the '327 patent's specification by, *inter alia*, non-limiting data from INCREASE showing that on a population basis, the use of Tyvaso in PH-ILD patients improved exercise capacity, improved six minute walk distance ('6MWD'), improved forced vital capacity ('FVC'), reduced exacerbations of ILD, and reduced levels of NT-proBNP in blood plasma." *Id*.
- "Claims 5, 6, 9 and 17 reflect clinical benefits that were observed on a population basis in INCREASE when Tyvaso was administered to PH-ILD patients." D.I. 426, 4.

Thus, Bayer's '310 patent and UTC's '327 patent both disclose and claim the same type of subject matter: the results of a phase III clinical trial.

Not only are the '310 and '327 patents directed to phase III clinical trial results, but the claims are similar. Both are method claims that require: a specific patient population; a specific drug or combination of drugs; and a specific dosing regimen. Accordingly, there is no room for

UTC to argue that the disclosure and claims of the '310 patent differ from the '327 patent in any material respect that would make the Federal Circuit's decision in *Bayer* inapplicable.

III. *BAYER PHARMA v. MYLAN* APPLIES TO CLAIMS 5, 6, 9 AND 17

A. The Federal Circuit's Analysis in *Bayer* Applies Here

In *Bayer*, the Federal Circuit affirmed, in relevant part, the PTAB's IPR final written decision ("FWD") that the phase "clinically proven effective" recited in claims 1 and 5 of U.S. Patent No. 10,828,310 ("the '310 patent") "fails to make the challenged claims patentable." *Bayer*, 2025 WL 2698408, at *2. Although *Bayer* was an appeal of an IPR FWD, the Federal Circuit reviewed the "clinically proven effective" issue de novo. *Id.* UTC cannot contend that the Federal Circuit's decision in *Bayer* is inapplicable here because of different burdens of proof.

Similar to *Bayer*, the measures of clinical effectiveness in claims 5, 6, 9 and 17 do not make the claims patentable. In its post-trial briefing on infringement, UTC asserted that the plain language of claims 5, 6, 9 and 17 does not include a step of measuring the recited clinical outcomes, and thus the claims do not require measuring any claimed outcome. D.I. 426, 8-9; D.I. 427, ¶ 6. Dr. Nathan testified that neither doctors nor patients need to measure the clinical outcomes, nor does a statistical analysis need to be performed. D.I. 425, ¶ 9; D.I. 424, 2. Dr. Nathan further testified that the claimed outcomes do not even need to be achieved because the "outcomes in claims 5, 6, 9, and 17 are the intended result of the dosing from Claim 1 in PH-ILD patients." D.I. 425, ¶ 9. Dr. Nathan went so far as to testify that claims 5, 6, 9 and 17 are "automatically" infringed if the method of claim 1 is performed. *Id.*, ¶ 10. Because UTC has advocated for a construction of claims 5, 6, 9 and 17 that removes any additional step, measurement, observation or even achieved outcome, the Federal Circuit's decision and supporting rationale in *Bayer* are applicable here and leads to the inescapable conclusion that these claims have no patentable weight. ¶

B. Like the "Clinically Proven Effective" Language in Bayer's '310 Patent, the Clinical Outcomes in Claims 5, 6, 9 and 17 Have No Functional Relationship to the Method of Claim 1

In *Bayer*, the Federal Circuit held that "clinically proven effective" is a "functionally unrelated limitation that fails to make the challenged claims patentable." *Bayer*, 2025 WL 2698408, at *2. Citing *King Pharms., Inc. v. Eon Lab'ys, Inc.*, 616 F.3d 1267, 1277-79 (Fed. Cir. 2010), which held that an otherwise anticipated method of treatment was not rendered patentable simply by "informing the patient," the Federal Circuit made clear that the relevant inquiry for determining whether claim language can breathe patentability into a claim is "whether the additional instructional limitation . . . [had] a 'new and unobvious functional relationship' with the known method of [treatment]." *Bayer*, 2025 WL 2698408, at *2. According to the Federal Circuit, the "rationale" underlying this inquiry is "preventing the indefinite patenting of known products [and methods] by the simple inclusion of novel, yet functionally unrelated limitations." *Id.* (quoting *King Pharms.*, 616 F.3d at 1279).

That rationale applies here. Even if no one was previously aware of the observed clinical outcomes of claims 5, 6, 9 and 17, these outcomes have no functional relationship to the known method of claim 1. UTC and Dr. Nathan have confirmed this to be true, as described above, based on their construction of these claims requiring, literally, nothing more than administering treprostinil to PH-ILD patients at the dosing required in claim 1. *See* D.I. 426, 4; D.I. 427, ¶ 6. Like Bayer, UTC is seeking to indefinitely patent a well-known and documented method by "simple inclusion" of clinical trial results from INCREASE.

Pointing again to *King Pharms.*, the Federal Circuit found it "equally troubling that one could claw back from the public domain an anticipated method of treatment merely by adding a limitation that the method subsequently performed well in a clinical trial." *Bayer*, 2025 WL

2698408, at *2. The rationale in *King Pharms.,* which the Federal Circuit applied in *Bayer*, applies equally here. As admitted by UTC, claims 5, 6, 9 and 17 claim nothing more than the "clinical benefits that were observed on a population basis in INCREASE when Tyvaso was administered to PH-ILD patients." D.I. 426, 4; D.I. 427, ¶ 6. That is the exact same type of limitation addressed in *Bayer*. And UTC, like Bayer, is seeking to claw back from the public domain the previously known method of claim 1 simply because this known method was performed in the INCREASE placebo-controlled trial. *See* D.I. 424, 1; D.I. 425, ¶ 108 (citing testimony from Drs. Waxman, Tapson and Hill that INCREASE confirmed their prior experience with Tyvaso to treat PH-ILD).

Bayer went further, concluding that the limitation requiring "clinical proof of efficacy . . . 'in no way transforms the process of taking the drug[s]' at the amounts and frequencies expressly recited in the claims." *Bayer*, 2025 WL 2698408, at *2 (quoting *King Pharms.*, 616 F.3d at 1279). This is because "'the actual method . . . is the same[.]'" *Id.* The same holds true for claims 5, 6, 9 and 17. Claim 1 of the '327 patent already specifies the dose of treprostinil to be administered to PH-ILD patients and the route of administration. JTX1, Claim 1. Claims 5, 6, 9 and 17 do not further define the drug, patient population, route of administration or dosage amounts, and thus the claimed method "is the same" as claim 1. *Id.*, Claims 5, 6, 9 and 17; D.I. 424, 3. Because claims 5, 6, 9, and 17 do not change the method of claim 1, they have no patentable weight.

C. *Bayer* Rejected Similar Arguments UTC Makes Here

In its appeal briefing, Bayer argued that the "clinically proven effective" limitation does change the steps of the claimed method (i.e., it adds a manipulative step to claim 1), asserting that before the COMPASS clinical trial, "administering the numerical amounts of rivaroxaban and aspirin in the claims would not have constituted administering clinically proven effective amounts

of rivaroxaban and aspirin." Ex. A (Bayer "Reply Brief of Appellant") at 6. According to Bayer, only by "proving in a clinical trial that the [claimed] numerical amounts of rivaroxaban and aspirin" are effective can one have a reasonable expectation of successfully achieving the "clinically proven effective" limitation and, as such, the phrase has patentable weight. *Id.* at 6-7. The Federal Circuit rejected Bayer's "a phase III clinical trial is necessary" argument, holding that even if "clinically proven effective," the limitation does not transform the process of taking the drugs in claim 1 or the recited doses, and thus the limitation does not add patentable weight. *Bayer*, 2025 WL 2698408, at *2-3 ("Because the claims of the '310 patent already specify the exact dosages [of drugs] to be administered to a patient, the additional limitation that the amounts be 'clinically proven effective' does not further define the dosages that are administered."). And it would remove from the public domain a known method based only on taking measurements during a successful clinical trial. *Id.*

UTC makes similar "manipulative steps" arguments here. UTC argues a randomized, placebo-controlled clinical trial is necessary because "the device, product, formulation, dosing, and course of treatment over time would all impact the results obtained when a patient administers according to the method in claim 1." D.I. 431, 4, 34. As such, according to UTC, the clinical observations in claims 5, 6, 9 and 17 do impart a manipulative difference, granting them patentable weight. *Id.* at 17. But like the "clinically proven effective" limitation in the Bayer '310 patent, none of claims 5, 6, 9, or 17 transform the process of taking treprostinil in claim 1, nor the recited doses—the method of treatment, as specified in claim 1, remains the same. Moreover, because claims 5, 6, 9 and 17 depend directly from claim 1, regardless of the device, product, formulation or specific dose of treprostinil administered between the "at least 15 micrograms up to a maximum tolerated dose," if claim 1 is infringed then, according to Dr. Nathan, the asserted dependent claims

are "automatically infringed."[1] This further confirms that claims 5, 6, 9 and 17 impart no functional limitation or manipulative difference to claim 1 and have no patentable weight.

Additionally, relying on *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370 (Fed. Cir. 2019), Bayer argued that "clinically proven effective" was material to the patentability of claims 1 and 5 because it described the invention. *See Bayer*, 2025 WL 2698408, at *3. The Federal Circuit disagreed because the claims at issue in *Allergan* included "functional limitations that limited the open-ended universe of potential compositions . . . by specifying safety and efficacy benchmarks the overall composition must meet." *Bayer*, 2025 WL 2698408, at *3. Specifically, in *Allergan Sales*, the Federal Circuit determined the "claimed invention is ultimately a formulation (and methods of using that formulation)" that differed from formulations and methods of the prior art because it allowed for "increased efficacy and safety." The patent expressly compared the claimed invention to the prior art and the "wherein" clause at issue related to whether patients could be safely and effectively treated twice a day rather than three times a day with the claimed formulation. 935 F.3d at 1375. In other words, the language in the claim directly affected and limited the claimed method. *Id.* at 1372-73. The Federal Circuit also relied on the specification's inclusion of Example II, a clinical trial that compared the claimed formulation to the prior art treatments, as well as Allergan's and the PTO Examiner's reliance on the impact the claimed formulation had on the course of treatment during prosecution to distinguish the claimed invention over the prior art and allow the claims. *Id.* at 1374-76. In contrast, "clinically proven effective" served no "analogous function" in the '310 patent claims because the '310 patent "already specif[ied] the exact dosages" to be administered to a patient and "clinically proven

[1] Claim 1 is not limited to a specific inhalation device, product, formulation, or course of treatment. JTX1, Claim 1.

effective" did not further define the administered doses or course of treatment. *Bayer*, 2025 WL 2698408, at *3.

Here, claims 5, 6, 9 and 17, like the '310 patent in *Bayer*, do not contain "functional limitations" that limit the drug, route of administration, doses or course of treatment recited in claim 1—they do nothing more than reflect a clinical observation achieved by following claim 1. D.I. 426, 4. And critically, unlike in *Allergan Sales*, where those safety and efficacy benchmarks had to be met to assess whether another method infringes, UTC has argued that no such requirement exists for claims 5, 6, 9 and 17. UTC offered no evidence at trial that when patients were treated with YUTREPIA, they achieved the measured outcomes of claims 5, 6, 9 and 17. And Dr. Nathan testified that: (1) neither NT-proBNP, FVC, exacerbations of ILD, FVC, nor 6MWD need to be measured and no statistical analysis needs to be performed (D.I. 425, ¶ 9 (citing Tr. 141:23-142:1, 142:18-24, 144:9-18, 153:8-11)); (2) a patient does not need to achieve the claimed outcome (*id.* (citing Tr. 142:13-17)); and (3) claims 5, 6, 9 and 17 are automatically infringed if the method of claim 1 is performed (*id.*, ¶ 10 (citing Tr. 142:7-12, 143:8-22)). Instead, UTC argued that these outcomes need never be measured in order to infringe, distinguishing the claims from *Allergan Sales*. D.I. 426, 4. Moreover, unlike *Allergan Sales*, none of claims 1, 5, 6, 9 or 17 of the '327 patent are formulation claims, the '327 specification contains no clinical trial comparing Tyvaso in PH-ILD to another treatment, and there is no evidence that either UTC or the Examiner relied on any of claims 5, 6, 9 or 17 as a basis for patentability and allowance. Thus, the Court should reject, like the Federal Circuit did with respect to the claims at issue in *Bayer*, any new attempt by UTC to analogize claims 5, 6, 9 and 17 to the claims in *Allergan Sales*. *Bayer* controls the inquiry here. Claims 5, 6, 9 and 17 do not manipulate or add any function limitation to claim 1 and thus carry no patentable weight.

IV. CONCLUSION

For the reasons discussed herein, the Federal Circuit's decision and supporting rationale in *Bayer*, is directly applicable to claims 5, 6, 9 and 17 of the '327 patent. *Bayer* supports Liquidia's position that claims 5, 6, 9 and 17 do not impart patentable weight to the known method of claim 1 and need not be considered when determining anticipation and obviousness of the '327 patent.

Respectfully submitted,

/s/ Nathan R. Hoeschen

Nathan R. Hoeschen (No. 6232)

Enclosures
cc: Clerk of the Court (by CM/ECF)
All counsel of record (by CM/ECF & Email)